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March 10, 2003

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Commissioner for Patents
Washington, D.C. 20231

Art Unit 1641

Re: U.S. Utility Patent Application
Appl. No. 09/975,133; Filed: October 10, 2001
For: **High Throughput Screening Assay Systems in Microscale Fluidic Devices**
Inventors: Parce *et al.*
Our Ref: 2052.002000B/LEA/EDH

RECEIVED

MAR 12 2003

Sir:

Transmitted herewith for appropriate action are the following documents:

TECH CENTER 1600/2900

1. Request by Applicants for Interference Under 37 C.F.R. § 1.607 and Statement Under 37 C.F.R. § 1.608(a), with Table 1 attached;
2. A copy of U.S. Patent No. 6,171,865 to Weigl *et al.*; and
3. A return postcard.

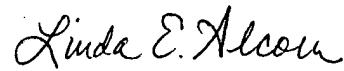
It is respectfully requested that the attached postcard be stamped with the date of filing of these documents, and that it be returned to our courier. In the event that extensions of time are necessary to prevent abandonment of this patent application, then such extensions of time are hereby petitioned.

Commissioner for Patents
March 10, 2003
Page 2

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Linda E. Alcorn
Attorney for Applicants
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LEA/EDH:nr
Enclosures
SKGF_DC1:109335.1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



In re application of:

Parce *et al.*

Appl. No.: 09/975,133

Filed: October 10, 2001

**For: High Throughput Screening Assay
Systems in Microscale Fluidic Devices**

Confirmation No.: 23447

Art Unit: 1641

Examiner: Christopher Chin

Atty. Docket: 2052.002000B/LEA/EDH

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REQUEST BY APPLICANTS FOR INTERFERENCE
UNDER 37 C.F.R. § 1.607 AND STATEMENT UNDER 37 C.F.R. § 1.608(a)

Assistant Commissioner for Patents
Washington, DC 20231

Sir:

Pursuant to the provisions of 37 C.F.R. § 1.607 and 1.643, Caliper Technologies Corp., assignee of record of the entire interest of the present application, requests the declaration of an interference between the present application and U.S. Patent No. 6,171,865 to Weigl *et al.*; issued on January 9, 2001 ("the Weigl '865 patent"). A copy of the Weigl '865 patent is enclosed.

I. PROPOSED COUNT

In accordance with 37 C.F.R. § 1.607(a)(2), the following count is proposed:

Proposed Count 1

A device for detecting the presence or determining the concentration of analyte particles in a sample stream comprising:

- a) a laminar flow channel;
- b) at least three inlet means in fluid connection with said laminar flow channel for respectively conducting into said laminar flow channel (1) an indicator stream, (2) a sample stream, and (3) a reference stream; and
- c) wherein said laminar flow channel has a dimension sufficiently small to allow laminar flow of said streams adjacent to each other and a length sufficient to allow analyte particles to diffuse from at least one

stream selected from the group consisting of said sample stream and said reference stream into the indicator stream to form at least one detection area.

Proposed Count 1 corresponds exactly to claim 1 of the Weigl '865 patent and claim 75 of the present application.

II. IDENTIFICATION OF CLAIMS CORRESPONDING TO PROPOSED COUNTS

A. Weigl '865 Patent Claims

Claim 1 of the Weigl '865 patent corresponds exactly to proposed Count 1. Claims 2-22 of the Weigl '865 patent correspond substantially to proposed Count 1, in the sense of 37 C.F.R. § 1.607(f) in that they are not identical to the count but define the same patentable invention under 37 C.F.R. § 1.607(n).

B. Claims of the present application

The present application, as amended in a Preliminary Amendment filed October 10, 2001, contains claims 75-93.

Claim 75 corresponds exactly to proposed Count 1. Claims 76-93 of the present application correspond substantially to proposed Count 1, in the sense of 37 C.F.R. § 1.607(f) in that they are not identical to the count but define the same patentable invention under 37 C.F.R. § 1.607(n).

III. APPLICATION OF CLAIMS 75-93 TO THE DISCLOSURE OF THE PRESENT APPLICATION

Attached Table 1 was submitted with the above-mentioned Preliminary Amendment.

Table 1 sets forth examples of support in the present specification for each claim feature of claims 75-93. Accordingly, the subject matter of claims 75-93 is disclosed in the present application at least according to Table 1.

IV. 35 U.S.C. § 135(b)

The claims identified as corresponding to the count were presented in a Preliminary Amendment filed October 10, 2001. As the Preliminary Amendment was filed within one (1) year of the issue date of the Weigl '865 patent, January 9, 2001, Applicants have complied with 35 U.S.C. § 135(b).

V. STATEMENT UNDER 37 C.F.R. § 1.608(a)

The present application is a continuation of Application No. 09/346,660, filed July 1, 1999, which is a continuation of Application No. 08/671,987, filed June 28, 1996. The present application claims the benefit under 35 U.S.C. § 120 of the earlier filing date of Application No. 08/671,987, filed June 28, 1996. Accordingly, the present application is entitled to an effective filing date of June 28, 1996.

The face of the Weigl '865 patent indicates that it was filed on August 4, 1999, and claims priority as a continuation of Application No. 08/900,926, filed July 25, 1997, now U.S. Patent No. 5,948,684, which claims priority as a continuation-in-part of Application No.

Parce *et al.*
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08/625,808, filed March 29, 1996, now U.S. Patent No. 5,716,852, and also as a continuation-in-part of Application No. 08/829,679, filed March 31, 1997, now U.S. Patent No. 5,972,710.

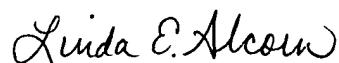
Without making an admission as to whether the claims of the Weigl '865 patent are entitled to priority, the earliest effective filing date to which the Weigl '865 patent *may be* entitled is March 29, 1996. Accordingly, the effective filing date of the present application is within three months of the potential earliest effective filing date of any claim of the Weigl '865 patent. In accordance with 37 C.F.R. § 1.608(a), Applicant's undersigned attorney of record hereby states that there is a basis upon which Applicants are entitled to a judgment relative to the patentee.

VI. CONCLUSION

For the foregoing reasons, it is respectfully requested that an interference be declared between the present application and the Weigl '865 patent.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



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Date: March 10, 2003

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TABLE 1



	U.S. Patent No. 6,171,865	Present Application
Claim 1 of '865 patent. Claim 75 in present application.	<p>1. A device for detecting the presence or determining the concentration of analyte particles in a sample stream comprising:</p> <p>a) a laminar flow channel;</p> <p>b) at least three inlet means in fluid connection with said laminar flow channel for respectively conducting into said laminar flow channel (1) an indicator stream, (2) a sample stream, and (3) a reference stream; and</p> <p>c) wherein said laminar flow channel has a dimension sufficiently small to allow laminar flow of said streams adjacent to each other and a length sufficient to allow analyte particles to diffuse from at least one stream selected from the group consisting of said sample stream and said reference stream into the indicator stream to form at least one detection area.</p>	<p>The present invention generally provides microfluidic devices for performing screening assays. For example, page 7, lines 3-9 generally describes microfluidic devices for screening compounds.</p> <p>Figure 1, element 110 illustrates a laminar flow channel on microfluidic device 102. See accompanying text on page 14, lines 27-30.</p> <p>Figure 2A, illustrates three inlet means, 104, 112 and 106 in fluid connection with a laminar flow channel 110 for conducting into the channel, an indicator stream such as a fluorogenic substrate, a sample stream for e.g., an enzyme stream and a reference stream, for e.g., a control compound with no effect on the enzyme/substrate complex, see accompanying text on page 23, line 19 through page 24, line 4.</p> <p>Page 14, lines 27-35 describe channels having cross sectional dimensions in the range of $0.1\mu\text{m}$ to about $500\mu\text{m}$. Therefore, the cross section of at least one channel will result in laminar flow of fluids within that channel. Example of this flow is described on page 23, line 19 through page 24, line 4 wherein a fluorogenic substrate, an enzyme and a test compound stream are flowed in a laminar flow within a channel to allow for particles from the test compound stream to diffuse into the fluorogenic stream.</p>
Claim 2 of '865 patent. Claim 76 in present application.	A device of claim 1/75 also comprising outlet means comprising branching channels for separation of the streams into one or more channels.	Figure 6A and page 33, lines 9 -26 describe a microfluidic device comprising branching channels for separation of the streams into one or more channels.
Claim 3 of '865 patent. Claim 77 in present application.	The device of claim 2/76 wherein said outlet means comprise smaller channels for conducting the sample stream than for conducting the indicator stream.	Page 34 lines 9-10 describes channels having varying geometries.
Claim 4 of '865 patent. Claim 78 in present application.	A device of claim 1/75 further comprising detecting means positioned relative to said flow channel such that said detecting means can detect a change in a detectable property in at least one of said streams.	A detection means is described on page 32 lines 23-25 and is illustrated in Figures 4E-4F. Also, Figure 6,element 662 illustrates a detection means positioned relative to a flow channel for detection of a change in a detectable property in at least one of the streams.

Claim 5 of '865 patent. Claim 79 in present application.	A device of claim 4/78 wherein said detecting means comprise components selected from the group consisting of a charge coupled device camera, a diode array detector, a fluorescence detector, and an electrochemical detector.	Page 17, lines 10-28 describes optical detection means such as fluorescence and electrochemical detectors.
Claim 6 of '865 patent. Claim 80 in present application.	A device of claim 1/75 further comprising inlet means for conducting at least one additional reference or sample stream in laminar flow contact with said indicator stream.	Figure 1, element 106, provides a source of at least one additional stream to flow through channel 112 which enters into laminar flow contact with indicator stream in channel 110.
Claim 7 of '865 patent. Claim 81 in present application.	A device of claim 1/75 further comprising means for dividing said indicator or sample stream into at least two separate streams and conducting said separate streams into said laminar flow channel.	Means for conducting and/or dividing flow of indicator or sample stream into at least two separate streams is described throughout the specification. For example, see page 33, line 30 through page 34, line 8 and page 34, lines 21-29.
Claim 8 of '865 patent. Claim 82 in present application.	A device of claim 1/75 further comprising a plurality of laminar flow channels in fluid communication with an indicator stream channel and means for conducting portions of an indicator stream from said indicator stream channel into laminar flow with separate sample or reference streams in said laminar flow channels.	Plurality of laminar flow channels connected to an indicator stream channel for conducting portion of the indicator stream into laminar flow with separate samples is illustrated in Figures 6A-C and described on pages 33, line 30 through page 34, line 8 and page 34, lines 21-29.
Claim 10 of '865 patent. Claim 83 in present application.	A method for detecting the presence or determining the concentration of analyte particles in a sample stream, comprising: a) conducting said sample stream into a laminar flow channel;	The present invention provides devices and methods for detecting the presence of analyte particles in a sample stream. See page 7, line 33 through page 8, line 3. Figure 5, element 512 and accompanying text on page 25, lines 35-37 describes conducting a sample stream into a laminar flow channel.
	b) conducting an indicator stream, said indicator stream comprising an indicator substance which indicates the presence of said analyte particles by a change in a detectable property when contacted with particles of said analyte, into said laminar flow channel, whereby said sample stream and said indicator stream flow in adjacent laminar flow in said channel;	Figure 5, and text on page 26, lines 12-15 illustrate conducting an indicator stream such as a labeled ligand into the laminar flow channel whereby, the indicator stream and the sample stream flow in adjacent laminar flow in the channel 510b

	c) conducting a reference stream, comprising a constant concentration of 0 or greater of reference particles into said laminar flow channel, whereby said reference stream flows in a laminar stream adjacent to said indicator stream;	Figure 5, page 25 lines 37-37, page 26, lines 6-15 and page 8, lines 29-32 describe flowing a control the laminar flow channel such that the control and the indicator stream flow adjacently in a laminar flow.
	d) allowing analyte particles to diffuse into said indicator stream;	Page 26, lines 6-10 describes the mixing of analyte particles from test compound into the indicator stream.
	e) allowing reference particles to diffuse into said indicator stream;	Page 26, lines 11-20 describe the mixing of the reference particles to diffuse into the indicator stream.
	f) detecting the presence or determining the concentration of said analyte and reference particles in said indicator stream; and	Detection of the presence of an analyte is described on pages 24, lines 15-18, page 25, lines 8-15 and is illustrated in Figure 5 as a detection window on channel 524.
	g) separately conducting at least one of said streams out of said laminar flow channel.	Page 26, lines 32-38 describes separately conducting the sample stream out of a reaction channel which is the laminar flow channel.
Claim 11 of '865 patent. Claim 84 in present application.	The method of claim 10/83, wherein the reference stream contains a concentration of analyte particles which is greater than zero.	Figure 2B, element 152 illustrates flowing test compounds or control streams into channel 112. Page 8, lines 29-32 describes a control sample that is used as a reference. See page 8, lines 29-32. Also see page 24, line 37 through page 25 line 8 for the description of different types of reference compounds.
Claim 13 of '865 patent. Claim 85 in present application.	The method of claim 10/83, wherein two reference streams are conducted into said laminar flow channel in adjacent laminar flow to said indicator stream.	Figure 2B illustrates the serial introduction of two reference plug streams into laminar flow channel wherein they are directed to flow in laminar flow adjacent to an indicator stream. See page 26, lines 11-20.
Claim 14 of '865 patent. Claim 86 in present application.	A method of claim 10/83, wherein said reference stream is a control stream.	See Figure 2B, element 152. See also page 24, line 36 through page 25, line 8.
Claim 15 of '865 patent. Claim 87 in present application.	A method of claim 10/83, wherein said reference stream is an internal standard stream.	The methods of the present invention describe internal standards such as spacer fluids that are be used as a standard for a constant signal. See page 24, lines 27-37.
Claim 16 of '865 patent. Claim 88 in present application.	A method of claim 15/87, wherein said internal standard stream contains reference particles different from said analyte particles.	See page 24, line 30 through page 25, line 3 for a description of a internal standard containing reference particles.

Claim 17 of '865 patent. Claim 89 in present application.	A method of claim 15/87, wherein said internal standard stream contains reference particles the same as said analyte particles.	See page 24, line 30 through page 25, line 3 for a description of a internal standard containing reference particles.
Claim 19 of '865 patent. Claim 90 in present application.	A method of claim 10/83, wherein said reference stream is used as a calibration stream.	See page 24, line 30 through page 25, line 4 for a description of a reference stream used as a calibration.
Claim 20 of '865 patent. Claim 91 in present application.	A method of claim 10/83 wherein the detectable property is selected from the group consisting of absorbance, chemiluminescence and fluorescence.	Page 17, lines 12-21 describes detectable properties such as fluorescence and absorbance.
Claim 21 of '865 patent. Claim 92 in present application.	A method of claim 10/83, wherein the indicator substance is immobilized on a particulate substance carried within the indicator stream.	Page 29, lines 26-31 illustrates an indicator substance immobilized on a particulate substance for e.g., a bead.
Claim 22 of '865 patent. Claim 93 in present application.	The method of claim 10/83 wherein step (g) comprises conducting the sample stream from said indicator stream.	Figure 5 illustrates conducting the sample stream from said indicator stream by flowing the sample stream out of laminar flow channel 510 into transfer channel 526. See accompanying text on page 26, lines 32-38.